Final Technical Report for DOE Grant DE-SC0018662

Project Name: ***Production and Separations for High Specific Activity ^{186}Re, ^{189}Re and ^{47}Sc for Research and Clinical Applications: effective design of targets and recycling of targets and radioisotope separation***

Report Date: February 2023

Federal Program Manager: Ethan Balkin

Work-scope Highlights: This grant involved three objectives for producing high specific activity radionuclides using reactor and accelerator technologies that would find use in medical, industrial and research applications. There was a strong emphasis in all projects to develop and train staff and students in all aspects of targetry, reactor and accelerator production, separation of radionuclides from enriched target material, and evaluating the specific activity of the product radionuclides. This grant formed a quadrilateral collaboration between the University of Missouri (MU), the University of Washington (UW), Brookhaven National Laboratory (BNL; separately funded), and Argonne National Laboratory (ANL; separately funded). All four institutions were involved in all projects, but to different degrees. The chemistry graduate students (Ph.D. program at MU) and the postdoctoral fellows (various institutions) may have participated in an internship at one or all of the other institutions for training and project translation/facilitation.

Specific Objective 1. *Optimize the targetry, production and separation for high specific activity ^{186}Re and ^{189}Re*. We were previously funded by the DOE Isotope Program (DE-SC0007348) to develop methods for producing high specific activity ^{186}Re. We determined that metallic W would likely make the best target material, and the current project aimed to scale up the accelerator production of high specific activity ^{186}Re for translation to quantities sufficient for research and clinical applications. During the irradiation of Os targets, we observed the production of ^{189}Re in reasonable quantities in a 16 MeV proton irradiation; SRIM calculations suggested that higher cross sections would be observed with 20-24 MeV protons for the ^{192}Os(p,α)^{189}Re reaction. This was to be evaluated with enriched ^{192}Os metal powder targets sandwiched between graphite. We also investigated electron LINAC production of ^{186}Re and ^{189}Re from Os targets by the (γ,p) reaction and reactor production via the ^{189}Os(n,p)^{189}Re reaction. The routine availability of high specific activity ^{186}Re and ^{189}Re will be of high interest to the research and clinical community as they are each a "matched pair" theranostic nuclide for ^{99m}Tc.

Milestones (MU)

1. *Identify graduate student(s) to work on the high specific activity $^{186/189}Re$ production project*. 5 graduate students and 2 undergraduate students contributed to this project.

2. *Continue to optimize the production and characterization of OsS_2 target material, including recycling enriched $^{189/192}OsS_2$ target material for reuse*. Some OsS_2 was sent to BNL for evaluation. The co-production of Ir radioisotopes made this route unfavorable.

3. *Conduct neutron irradiations on small ^{189}Os metal powder targets in the flux trap at MURR to determine the feasibility of the $^{189}Os(n,p)^{189}Re$ production route; determine yields and radionuclidic purity*. The fast neutron energies at MURR and from the 16 MeV PETtrace were not sufficient for this reaction at MU.

4. *Conduct proton irradiations on $^{nat}WS_2$ target material to determine the optimal irradiation conditions for ^{186}Re production and to provide radiotracer rhenium for separation method analyses; gamma spectroscopy (HPGe) will be used for monitoring*. Completed for numerous studies. Manuscript(s) published.

5. *Conduct proton irradiations on $^{186}WS_2$ target material to confirm the optimal conditions (irradiation time, target geometry, cross section, and energy) for production of ^{186}Re; evaluate for yield and radionuclidic purity*. Completed. Manuscript(s) published.

Milestones (UW)

1. *Identify a postdoctoral fellow to work on the high specific activity $^{186/189}Re$ production project*. 3 postdoctoral fellows contributed to this project.

2. *Evaluate production and isolation yields for deuteron irradiations of graphite-encased W metal at higher beam currents (30 and 35 μA) than previously studied*. While we have not conducted deuteron irradiations at 30 μA or higher beam currents, deuteron irradiations of graphite-encased W have been conducted with a 22 MeV deuterium beam at 27 μA for 2 h to reproduce the experiment reported by our group previously (*Radiochim. Acta* **2017**, *105(12)*, 1071-1081 2017) and to further the irradiation times.

   Several technical factors precluded us from obtaining this goal, but important advances were made in our irradiation facilities and in the target used for irradiations that move us close to this goal. A new beamline was built to allow higher energy deuteron irradiations and a new target station was installed at the end of 2022. Deuteron beam tuning on the new beamline has not been conducted yet, but a higher beam current (30 and 35 μA) should be achieved after that is done in the near future. Irradiations for production of ^{186}Re using graphite-encased W metal targets at 30 μA and higher are planned at UW under other funding.

3. *Evaluate WS_2 target material (developed by MU) for the production of HSA ^{186}Re via the $^{186}W(d,2n)$ reaction*. Natural WS_2 targets were irradiated with 22 MeV deuteron beams at at 5 μA and 10 μA for 15 min to determine the stability of the target material with production rates of 60.8 and 80.6 μCi/μAh observed, respectively. A lower production rate from the first target was obtained because not all target material could be dissolved. A burn mark was observed on the Si cover. This might be due to high thermal contact resistance between the Si wafer and the WS_2, or low thermal conductivity of WS_2.

4. *Evaluate WS_2 target material (developed by MU) for the production of HSA ^{189}Re via the $^{186}W(\alpha,p)$ reaction*. Three enriched [^{186}W]WS_2 targets were irradiated to determine ^{189}Re production rate and radioisotopic/radionuclidic purity at different alpha beam energies. A

manuscript entitled "*Production rates of rhenium-189 from alpha irradiated natural and enriched tungsten disulfide thick targets*" is being prepared to report our findings from this work.

Specific Objective 2. *Optimize the targetry, production and separation of high specific activity ^{47}Sc*. We will determine the feasibility of producing high specific activity ^{47}Sc using both reactor and accelerator production methods; develop targetry, production and dissolution techniques; evaluate separation methods of ^{47}Sc from natural and enriched Ti target material, particularly those that will allow for recovery of the target. The nuclear properties of ^{47}Sc make it a desirable potential theranostic radionuclide.

Milestones (MU)

1. *Scandium-47 production via the $^{47}Ti(n,p)^{47}Sc$ reaction*. Following initial investigations, this milestone was not pursued at MU.

Specific Objective 3. *Training of graduate and postdoctoral Students*. We will train graduate and postdoctoral students in radiochemical methods for production and processing of these radionuclides. The proposed radionuclides present their own unique separation challenges due to available oxidation states and target material requirements. Through this joint program, the graduate student and postdoctoral fellow trainees will have a unique exposure to a range of accelerator facilities and challenging inorganic radiochemistry on which to develop their expertise. The goal of this objective was to train graduate students and postdoctoral students in radiochemical methods, for production of radionuclides and isolation/separation of the radionuclides from their target materials, and recovery/recycling of the target materials.

One graduate student from MU was awarded a DOE SCGSR fellowship to perform additional studies at BNL to evaluate W/Os targets at higher beam currents and proton/neutron energies.

One graduate student from MU spent 2 weeks working at UW to carry out experiments and obtain cross training. A manuscript is in preparation from this work.

Six graduate students were involved in this project. Three of them have earned their PhD degrees and moved on to postdoctoral positions. The other three graduate students continue at MU. Two undergraduate students worked on this project and are now in graduate programs. Three postdoctoral fellows worked on this project.

Education and Training:

Postdoctoral Fellows: 3 postdoctoral fellows at UW

Graduate Students: 6 graduate students at MU

Undergraduate Students: 2 undergraduate students at MU

Published Papers and Manuscripts in preparation/submitted:

"Bulk Production and Evaluation of High Specific Activity ^{186g}Re for Cancer Therapy Using Enriched $^{186}WO_3$ Targets in a Proton Beam", *Nucl. Med. Biol.* **2017**, *49*, 24-29 (from previous Re DOE grant but published after its completion)

"Chemistry and Radiochemistry of Arsenic, Rhenium and Rhodium Isotopes Relevant to Radiopharmaceutical Applications: Development of High Specific Activity Radionuclides for Imaging and Treatment", *Dalton Trans.* **2017**, *46*, 14677-14690 (DOI: 10.1039/c7dt02407; invited; from previous Re DOE grant but published after its completion)

"Scale-up of high specific activity ^{186}Re production using graphite-encased thick ^{186}W targets and demonstration of an efficient target recycling process", *Radiochim. Acta* **2017**, *105(12)*, 1071-1081.

"Radionuclide Production and Separation Techniques for Radiopharmaceutical Development and Nuclear Waste Processing", Ph.D. dissertation, University of Missouri, May **2018**.

"Chelators and Metal Complex Stability for Radiopharmaceutical Applications", *Radiochim. Acta* **2019**, 107(9-11), 1087-1120 (invited; DOI 10.1515/ract-2018-3090).

"Theranostic and Matched Pair Radionuclides as Radiopharmaceutical for Imaging and Radiotherapy", Ph.D. dissertation, University of Missouri, December **2020**.

"Evaluation of $^{186}WS_2$ target material for production of high specific activity ^{186}Re via proton irradiation: Separation, radiolabeling and recovery/recycling", Radiochim. Acta **2022**, 110(6-9), 739-749 (https://doi.org/10.1515/ract-2021-1138).

"Production of High Specific Activity Rhenium-186 for Radiotherapeutic Applications and Reformulation of a Novel Liquid Brachytherapy Agent", Ph.D. dissertation, University of Missouri, July **2022**.

"Evaluation of the photonuclear production of radiorheniums from natural osmium targets", **2022**, to be submitted to Applied Radiation and Isotopes.

We are working on 1-2 additional Re manuscripts from this project.

Presentations at Meetings/Conferences:

"Synthesis and evaluation of MAMA-based bifunctional chelators for the oxorhenium (V) core", presented at the *255th American Chemical Society Meeting*, 18-22 March 2018, New Orleans, LA (oral).

"Radiometals in diagnostic and therapeutic radiopharmaceutical applications", presented at the 255th American Chemical Society Meeting, 18-22 March 2018, New Orleans, LA (invited).

"Production of ^{186}Re and ^{189}Re from Enriched ^{189}Os and ^{192}Os Targets", presented at the *22nd International Symposium on Radiopharmaceutical Sciences (ISRS2017)*, 14-19 May 2017, Dresden, Germany.

"The long and exciting road in technetium and rhenium chemistry", presented at TERACHEM 2018, 26-29 September 2018, Bressanone, Italy (invited; TERACHEM 2018 Award lecture).

"Medical radionuclide production research at the University of Washington: Facilities and cyclotron produced medical radionuclides", presented at the *260th ACS National Meeting held in San Francisco (virtually)* 23-26 August 2020.

"Production of High Specific Activity Rhenium Radioisotopes for Radiotherapeutic Applications", presented at the *261st National Virtual Meeting of the American Chemical Society*. 5-16 April 2021.

"Production of High Specific Activity Rhenium-186 via the ^{186}W(d,2n)^{186}Re Nuclear Reaction Using Pressed Tungsten-186 Metal Targets and Evaluation of Separation Methods", presented at the *261st National Virtual Meeting of the American Chemical Society*. 5-16 April 2021.

"A Comparison of Rhenium Isolation and Tungsten Recovery Methods from Bulk Tungsten Targets.", presented at the *eSRS, Virtual Meeting*. May 17-19, 2021.

"High Specific Activity Radiometal and Radiometalloid Chemistry for Development of Potential Radiopharmaceuticals", Lind Award Lecturer (ACS, Eastern Tennessee Section), Oak Ridge National Laboratory, 11 May 2022.